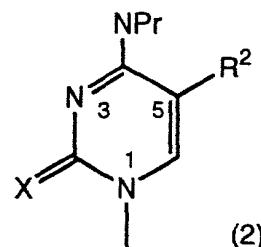
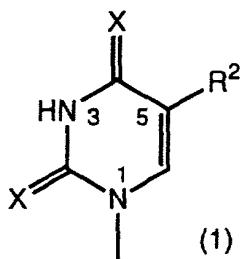


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CLAIMS

1. An oligomer comprising at least two nucleomonomers and pharmaceutically acceptable salts  
5 thereof wherein at least one of said nucleomonomers comprises a base of formula (1) or (2):

10



15

wherein each X is independently O or S;  
R<sup>2</sup> is a group comprising at least one pi bond connected to the carbon atom attached to the base; and  
Pr is (H), or a protecting group,  
20 with the proviso that when at least one of said nucleomonomers of said oligomer comprises deoxyuridine 5-substituted by vinyl, 1-butenyl, 1-pentenyl, 1-hexenyl, 1-heptenyl, 1-octenyl, 1-propynyl, 1-butynyl, 1-hexynyl, 1-heptynyl, or 1-octynyl, then the remainder of the  
25 nucleomonomers comprising said oligomer are not solely comprised of phosphodiester linked 2'-deoxyadenosine, 2'-deoxyguanosine, 2'-deoxycytidine, thymidine or a combination thereof.

30

2. The oligomer of claim 1 wherein X is O.

35

3. The oligomer of claim 1 or 2 wherein R<sup>2</sup> is not phenyl.

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4. The oligomer of claim 1 or 2 wherein R<sup>2</sup> is cyano, C<sub>2-12</sub> 1-alkenyl or 1-alkynyl or is a C<sub>2-12</sub> heteroaromatic or 1-ethynyl-heteroaromatic group containing 5-6 ring atoms in which one to three of the 5 ring atoms is N, S or O.

5. The oligomer of claim 4 wherein R<sup>2</sup> is C<sub>2-8</sub> 1-alkenyl or 1-alkynyl or is a C<sub>2-8</sub> heteroaromatic or 1-ethynyl-heteroaromatic group containing 5-6 ring atoms in 10 which one ring atom is replaced by N and optionally in which a second ring atom is N, S or O.

6. The oligomer of claim 5 wherein R<sup>2</sup> is selected from the group consisting of phenylethynyl, 2-, 15 3-, and 4-pyridine-ethynyl, 2-, 4- and 5-pyrimidine-ethynyl, triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and 5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and 20 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-, 4-, and 5-oxazolyl, 2- and 3-furanyl, 2- and 3-pyrrolyl, propenyl, vinyl and -C≡C-Z where Z is H, alkyl (C<sub>1-10</sub>), 25 haloalkyl (C<sub>1-10</sub> with 1 to 6 halogen atoms) or heteroalkyl (C<sub>1-10</sub> with 1 to 3 heteroatoms).

7. The oligomer of claim 1 wherein R<sup>2</sup> is selected from the group consisting of 1-propynyl, 1-propenyl, 3-buten-1-ynyl, 3-methyl-1-butynyl, 30 3,3-dimethyl-1-butynyl, 1,3-pentadiynyl, 1-butynyl, ethynyl, vinyl, bromovinyl, phenylethynyl, 2-, 3-, and 4-pyridine-ethynyl, 2-, 4- and 5-pyrimidine-ethynyl, 35

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triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and 5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-, 4-, and 5-oxazolyl, 2- and 3-furanyl, and 2- and 3-pyrrolyl.

10

8. The oligomer of claim 1 wherein R<sup>2</sup> is 1-propynyl.

15 9. The oligomer of claim 8 wherein at least one substitute linkage is a phosphorothioate linkage.

10. The oligomer of claim 9 wherein all substitute linkages are phosphorothioate linkages.

20

11. The oligomer of claim 1 wherein at least one substitute linkage is a phosphorothioate linkage.

12. The oligomer of claim 11 wherein all substitute linkages are phosphorothioate linkages.

25

13. The oligomer of claim 1 wherein at least one linkage is a substitute linkage.

30

14. The oligomer of claim 13 wherein the substitute linkage is selected from the group consisting of phosphoramidate, phosphorothioate, methylphosphonate, riboacetal, amide, N-methylhydroxylamine,

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thionomethylphosphonate, phosphorodithioate, 2',5' linkages, formacetal, and 3'-thioformacetal.

15. The oligomer of claim 14 wherein said  
5 substitute linkage is methylphosphonate or phosphorothioate.

16. The oligomer of claim 3 wherein at least one substitute linkage is a phosphorothioate linkage.

10

17. The oligomer of claim 16 wherein all substitute linkages are phosphorothioate linkages.

18. The oligomer of claim 3 wherein at least  
15 one linkage is a substituted linkage.

19. The oligomer of claim 18 wherein the substitute linkage is selected from the group consisting of phosphoramidate, phosphorothioate, methylphosphonate,  
20 riboacetal, amide, N-methylhydroxylamine, thionomethylphosphonate, phosphorodithioate, 2',5' linkages, formacetal, and 3'-thioformacetal.

20. The oligomer of claim 19 wherein said  
25 substitute linkage is methylphosphonate or phosphorothioate.

21. The oligomer of claim 1 that further comprises at least one segment of inverted polarity.

30

22. The oligomer of claim 21 that further comprises at least one o-xyloso switchback linker.

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23. The oligomer of claim 22 wherein the  $\alpha$ -xyloso switchback linker comprises at least one base of formula (1) or (2) as defined in claim 1.

5 24. The oligomer of claim 1 wherein at least one base comprises a covalent bonding moiety.

10 25. The oligomer of claim 24 wherein said base is  $N^4,N^4$ -ethanocytosine.

15 26. The oligomer of claim 1 complexed with a cationic lipid.

20 27. The oligomer of claim 1 further comprising from about 10 to about 30 nucleomonomers and having uniform polarity.

25 28. The oligomer of claim 27 further comprising about 2 to about 12 substituted linkages or nucleomonomers at the 5'- end and at the 3'- end which comprise nuclease stable domains, and about 3 to about 26 substituted linkages or nucleomonomers which comprise at least one RNase H competent domain and is between the nuclease stable domains.

30 29. The oligomer of claim 3 complexed with a cationic lipid.

35 30. The oligomer of claim 3 further comprising from about 10 to about 30 nucleomonomers and having uniform polarity.

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31. The oligomer of claim 4 wherein said nucleomonomer is a 2'- modified nucleomonomer.

5 32. The oligomer of claim 31 wherein at least one of the nucleomonomer is a 2'-O-allyl modified nucleomonomer.

10 33. The oligomer of claim 1 having a covalent link between the 5' nucleomonomer and the 3' nucleomonomer whereby a circular oligomer is formed.

34. The oligomer of claim 1 conjugated to a solid support, label, or amine linker (1-12C).

15 35. The oligomer of claim 1 which is a dimer, trimer, tetramer, pentamer or hexamer.

20 36. The oligomer of claim 3 conjugated to a solid support, label, or amine linker (1-12C).

37. The oligomer of claim 3 which is a dimer, trimer, tetramer, pentamer or hexamer.

25 38. An oligomer of claim 1 comprising a positive modification comprising at least one base of formula (1) or (2) and a negative modification, with respect to the binding affinity of the oligomer to a complementary nucleic acid sequence, wherein the positive modification counteracts the effect of the negative 30 modification to a degree that is more than additive with respect to the binding affinity.

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39. The oligomer of claim 38 wherein the positive modification  $R^2$  is cyano,  $C_{2-12}$  1-alkenyl or 1-alkynyl or is a  $C_{2-12}$  heteroaromatic or 1-ethynyl-heteroaromatic group containing 5-6 ring atoms in which 5 one to three of the ring atoms is independently N, S or O.

40. The oligomer of claim 39 wherein the heterocycle base modification  $R^2$  is  $C_{2-8}$  1-alkenyl or 1-alkynyl or is a  $C_{2-8}$  heteroaromatic or 1-ethynyl-heteroaromatic group containing 5 to 6 ring atoms in which one ring atom is N and optionally in which a second ring atom is N, S or O and each X is O.

41. The oligomer of claim 37 wherein the negative modification is a substitute linkage.

42. The oligomer of claim 41 wherein the substitute linkage comprises at least one linkage selected from the group consisting of phosphorothioate, thionomethylphosphonate, methylphosphonate, phosphoroamidate and triester for a phosphodiester linkage.

43. The oligomer of claim 1 wherein at least one  $R^3$  is O-methyl, O-ethyl or O-propyl.

44. The oligomer of claim 3 wherein at least one  $R^3$  is O-methyl, O-ethyl or O-propyl.

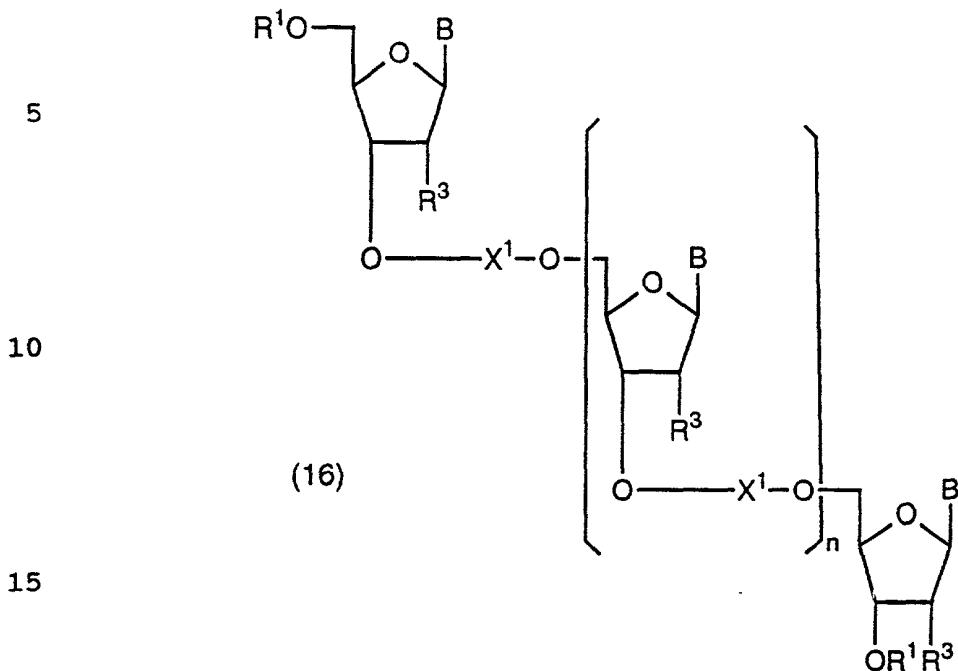
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45. An oligomer of the formula (16):

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wherein each R<sup>1</sup> is independently H, PO<sub>3</sub><sup>-2</sup>, or a  
20 blocking group;

each R<sup>3</sup> is independently selected from the  
group consisting of H, OH, F, NH<sub>2</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, OC<sub>3</sub>H<sub>7</sub>, SCH<sub>3</sub>,  
SC<sub>2</sub>H<sub>5</sub>, SC<sub>3</sub>H<sub>7</sub>, OC<sub>3</sub>H<sub>5</sub>, and SC<sub>3</sub>H<sub>5</sub>;

each X<sup>1</sup> is independently a substitute linkage  
25 selected from the group consisting of -P(S)(O)-,  
-P(O)(O)-, -P(Me)(O)- and -P(Me)(S)-.

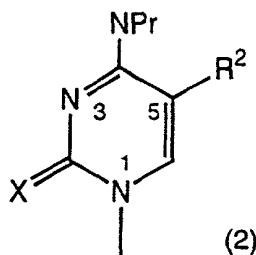
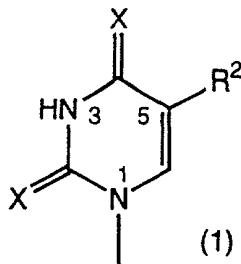
Pr is a protecting group;

n is an integer from 0 to 98; and

30 B is a purine or pyrimidine base, provided that  
at least one B is of formula (1) or (2):

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5



10

wherein each X is independently O or S; R<sup>2</sup> is a group comprising at least one pi bond connected through a carbon attached to the base; and

15

Pr is H<sub>2</sub> or a protecting group and with the proviso that when at least one of said nucleomonomers of said oligomer comprises deoxyuridine 5-substituted by vinyl, 1-butenyl, 1-pentenyl, 1-hexenyl, 1-heptenyl, 1-octenyl, 1-propynyl, 1-butynyl, 1-hexynyl, 1-heptynyl, or 1-octynyl, then the remainder of the nucleomonomers comprising said oligomer are not solely comprised of phosphodiester linked 2'-deoxyadenosine, 2'-deoxyguanosine, 2'-deoxycytidine, thymidine or a combination thereof.

20

46. The oligomer of claim 45 wherein at least one B is 5-propynyluracil, 5-(3-methyl-1-butynyl)uracil, 5-propynylcytosine or 5-(3-methyl-1-butynyl)cytosine.

25

47. The oligomer of claim 45 wherein at least one B is 2-thienyluracil, 2-thienylcytosine, 2-imidazoyluracil, 2-imidazoylcytosine, 2-thiazoyluracil or 2-thiazoylcytosine.

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48. The oligomer of claim 45 wherein at least one R<sup>1</sup> is H, PO<sub>3</sub><sup>2-</sup>, DMT, MMT, H-phosphonate, methyl phosphonamidite, methylphosphoramidite,  $\beta$ -cyanoethylphosphoramidite or alkylphosphoramidite.

5

49. The oligomer of claim 45 wherein each R<sup>3</sup> is independently H, OH, or -O-allyl.

10 50. The oligomer of claim 50 wherein at least one R<sup>3</sup> is O-methyl, O-ethyl or O-propyl.

51. The oligomer of claim 45 wherein R<sup>2</sup> is 1-propynyl.

15 52. The oligomer of claim 51 further comprising from about 10 to about 30 nucleomonomers and having uniform polarity and further comprising about 2 to about 12 substituted linkages or nucleomonomers at the 5'- end and at the 3'- end which comprise nuclease stable domains, and about 3 to about 26 substituted linkages or nucleomonomers which comprise at least one RNase H competent domain and is between the nuclease stable domains.

25 53. The oligomer of claim 45 complexed with a cationic lipid.

54. The oligomer of claim 46 wherein the cationic lipid is DOTMA.

30

55. The oligomer of claim 45 wherein R<sup>2</sup> is not phenyl.

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56. The oligomer of claim 55 wherein at least one R<sup>1</sup> is H, PO<sub>3</sub><sup>2-</sup>, DMT, MMT, H-phosphonate, methyl phosphonamidite, methylphosphoramidite,  $\beta$ -cyanoethylphosphoramidite or alkylphosphoramidite.

5

57. The oligomer of claim 55 wherein each R<sup>3</sup> is independently H, OH, or -O-allyl.

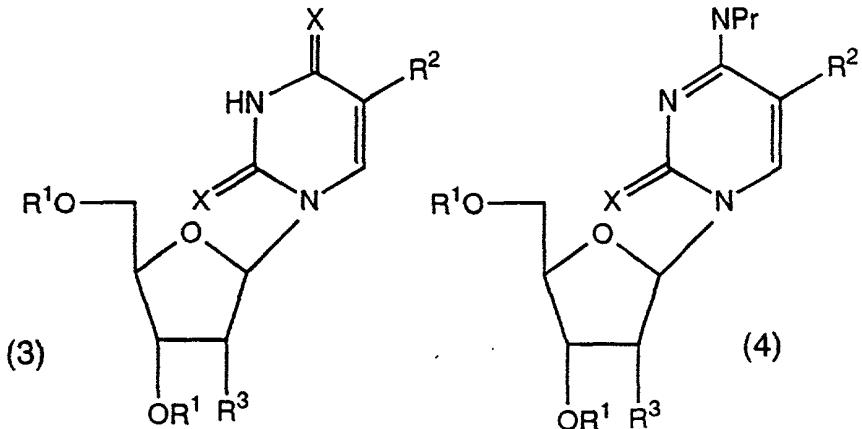
10 58. The oligomer of claim 55 wherein at least one R<sup>3</sup> is O-methyl, O-ethyl or O-propyl.

59. The oligomer of claim 55 complexed with a cationic lipid.

15 60. The oligomer of claim 59 wherein the cationic lipid is DOTMA.

20 61. A nucleomonomer having the structural formula (3) or (4):

25



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wherein each  $R^1$  is independently H or a blocking group;

$R^2$  is a group comprising at least one pi bond connected through a carbon atom attached to the base;

5  $Pr$  is  $(H_2)$  or a protecting group; and

$R^3$  is selected from the group consisting of H, OH, F,  $OCH_3$ ,  $OC_2H_5$ ,  $OC_3H_7$ ,  $SCH_3$ ,  $SC_2H_5$ ,  $SC_3H_7$ ,  $OC_3H_5$ , and  $SC_3H_5$ ,

with the proviso that if  $R^3$  is H or OH, and both  $R^1$  are H,  $R^2$  is 1,3-pentadiynyl, 2-, 3-, and 4-

10 pyridine-ethynyl, 2-pyrimidine-ethynyl, 4-pyrimidine-ethynyl, 5-pyrimidine-ethynyl, triazine-ethynyl, 2-

pyrimidinyl, 2- and 4-imidazolyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-thienyl-

ethynyl, 2-, 4- and 5-imidazolyl-ethynyl, 2-, 4-, and 5-

15 thiazolyl-ethynyl, 2-, 4- and 5-oxazolyl-ethynyl, 4- and 5-thiazolyl, 4- and 5-oxazolyl, or 3-pyrrolyl.

62. The nucleomonomer of claim 61 wherein  $Pr$  is  $(H_2)$ .

20

63. The nucleomonomer of claim 61 wherein  $R^2$  is 1-propynyl, 1-propenyl, 3-buten-1-ynyl, 3-methyl-1-butynyl, 3,3-dimethyl-1-butynyl, 1,3-pentadiynyl, 1-butynyl, ethynyl, vinyl, bromovinyl, phenylethynyl, 2-, 3-, and 4-pyridine-ethynyl, 2-, 4- and 5-pyrimidine-ethynyl, triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and 5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-,

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4-, and 5-oxazolyl, 2- and 3-furanyl, or 2- and 3-pyrrolyl; and

the blocking group is DMT, MMT, FMOC, hydrogen phosphonate, methylphosphonamidite, methylphosphoramidite or  $\beta$ -cyanoethylphosphoramidite.

64. The nucleomonomer of claim 63 wherein  $R^3$  is H, OH or O-allyl.

10 65. The nucleomonomer of claim 63 wherein  $R^2$  is 1-propynyl.

15 66. The nucleomonomer of claim 63 wherein  $R^1$  at the 3' position is selected from the group consisting of hydrogen phosphonate, N,N-diisopropylamino- $\beta$ -cyanoethoxyphosphine, N,N-diisopropyl-aminomethoxyphosphine, N,N-diethylamino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino-methoxyphosphine, N,N-diisopropylaminomethyl-  
20 phosphonamidite, N,N-diethylamino-methylphosphonamidite, bis-morpholino-phosphine, N,N-dimethylamino- $\beta$ -cyanoethyl-mercaptophosphine, 2-chlorophenyl phosphate, 4-chlorophenyl phosphate, 2,4-dichlorophenyl phosphate, 2,4-dibromophenyl phosphate, 2-chlorophenyl thiophosphate, 4-chlorophenyl thiophosphate, 2,4-dichlorophenyl thiophosphate, and 2,4-dibromophenyl phosphate.

25 67. The nucleomonomer of claim 61 wherein  $R^2$  is 1-propynyl.

30 68. The nucleomonomer of claim 61 wherein X is  
35 O;

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R<sup>1</sup> at the 5' position is DMT, MMT or FMOC;

R<sup>1</sup> at the 3' position is N,N-diisopropylamino- $\beta$ -cyanoethoxyphosphine, N,N-diisopropylaminomethoxyphosphine or hydrogen phosphonate;

5 R<sup>2</sup> is 1-propynyl, 3-methyl-1-butynyl, 2-thienyl, 2-imidazolyl or 2-thiazolyl;

R<sup>3</sup> is H, OH, or O-allyl; and

Pr is (H)<sub>2</sub>, diisobutylformamidine or another protecting group.

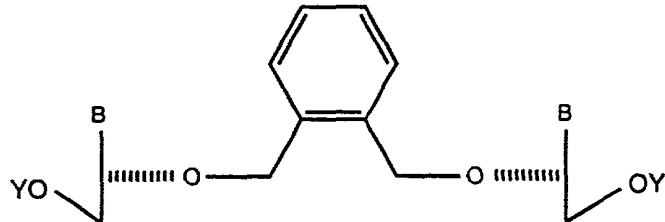
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69. The nucleomonomer of claim 68 wherein Pr is benzoyl, diisopropylformamidine, FMOC, di-n-butylformamidine, or isobutyryl.

15

70. An o-oxyloso dimer of the formula (5):

20



(5)

25

wherein

each Y is independently R<sup>1</sup> or an oligomer;

R<sup>1</sup> is H, PO<sub>3</sub><sup>2-</sup> or a blocking group; and

30 each B is independently a purine or pyrimidine base, provided that at least one B is a base of formula (1) or (2), wherein R<sub>2</sub> is a group comprising at least one pi bond connected through a carbon atom attached to the base; and Pr is (H)<sub>2</sub> or a protecting group.

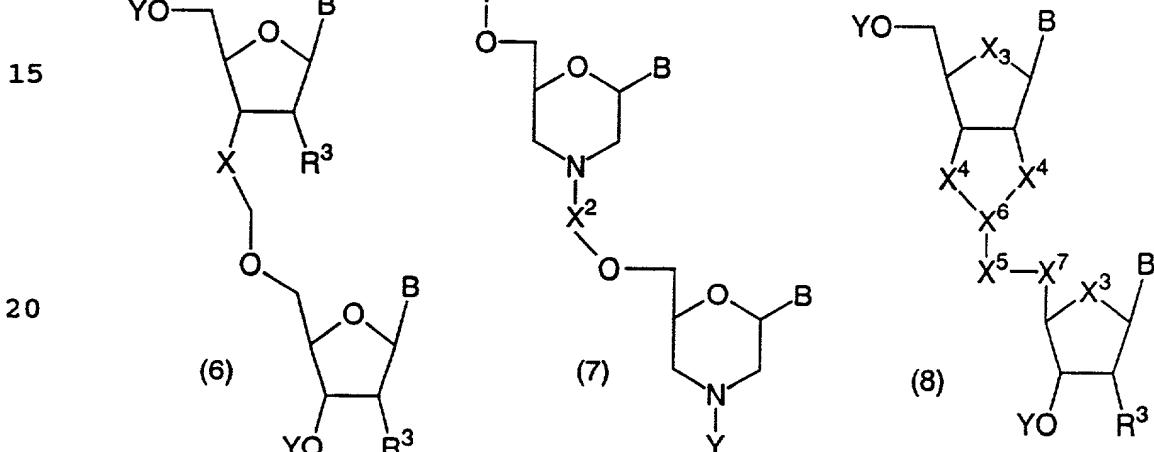
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71. The dimer of claim 70 wherein R<sup>2</sup> is 1-propynyl.

5 72. The dimer of claim 70 wherein the blocking group is selected from the group consisting of DMT, MMT, hydrogen phosphonate, methylphosphonamidite, methylphosphoramidite, and  $\beta$ -cyanoethylphosphoramidite.

10 73. A dimer of the formula (6), (7) or (8):



wherein

30 X is selected from the group consisting of O and S;

X<sup>2</sup> is selected from the group consisting of CO, CS and SO<sub>2</sub>;

35 X<sup>3</sup> is independently selected from the group consisting of O, S, CH<sub>2</sub>, CF<sub>2</sub> and CFH;

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X<sup>4</sup> is independently selected from the group consisting of O, S, SO, SO<sub>2</sub>, CH<sub>2</sub>, CO, CF<sub>2</sub>, CS, NH and NR<sup>4</sup> wherein R<sup>4</sup> is lower alkyl (C<sub>1-4</sub>; methyl, ethyl, propyl, isopropyl, butyl or isobutyl);

5 X<sup>5</sup> is selected from the group consisting of O, CO, S, CH<sub>2</sub>, CS, SO<sub>2</sub>, CO, NH and NR<sup>4</sup>;

X<sup>6</sup> is selected from the group consisting of CH, N, CF, CCl, and CR<sup>5</sup> wherein R<sup>5</sup> is lower alkyl (C<sub>1-4</sub>) fluoromethyl, difluoromethyl, trifluoromethyl or lower 10 fluoroalkyl (C<sub>2-4</sub>, F<sub>1-5</sub>);

X<sup>7</sup> is selected from the group consisting of O, S, CH<sub>2</sub>, CO, CF<sub>2</sub> and CS;

each Y independently is an oligomer or R<sub>1</sub> wherein R<sub>1</sub> is PO<sub>3</sub><sup>-2</sup> or a blocking group;

15 each R<sup>3</sup> is independently selected from the group consisting of H, OH, F, NH<sub>2</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, OC<sub>3</sub>H<sub>7</sub>, SCH<sub>3</sub>, SC<sub>2</sub>H<sub>5</sub>, SC<sub>3</sub>H<sub>7</sub>, OC<sub>3</sub>H<sub>5</sub>, and SC<sub>3</sub>H<sub>5</sub>;

20 each B is independently a purine or pyrimidine base, provided that at least one B is of formula (1) or (2) wherein each X is O or S;

R<sub>2</sub> is a group comprising at least one pi bond connected through a carbon atom attached to the base; and

Pr is (H)<sub>2</sub> or a protecting group;

25 and further provided that X<sup>5</sup> and X<sup>7</sup> are not both O.

74. The dimer of claim 73 wherein R<sup>1</sup> is PO<sub>3</sub><sup>-2</sup>, DMT, MMT, H-phosphonate, methylphosphoramidite or β-cyanoethylphosphoramidite.

30 75. The dimer of claim 73 wherein at least one B is 5-propynyluracil, 3-methyl-1-butynyluracil, 5-propynylcytosine, or 3-methyl-1-butynylcytosine.

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76. The dimer of claim 73 wherein at least one R<sup>2</sup> is propynyl, R<sup>3</sup> is H or OH and X in the substitute linkage is S.

5

77. The dimer of claim 73 of formula (8) wherein X<sup>3</sup> and X<sup>4</sup> are O, X<sup>5</sup> and X<sup>7</sup> are CH<sub>2</sub>, and X<sup>6</sup> is CH.

78. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 1.

10

79. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 45.

15

80. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 1.

20

81. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 45.

82. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 3.

25

83. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 55.

30

84. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 3.

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85. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 55.

5 86. The oligomer of claim 1 wherein the oligomer persists intact in cells or biological solutions for a period of time that is greater than a corresponding oligodeoxynucleotide.

10 87. The oligomer of claim 3 wherein the oligomer persists intact in cells or biological solutions for a period of time that is greater than a corresponding oligodeoxynucleotide.

15 88. The oligomer of claim 1 wherein the oligomer is a ribozyme.

89. The oligomer of claim 3 wherein the oligomer is a ribozyme.

20 90. The oligomer of claim 1 wherein the oligomer is a probe.

91. The oligomer of claim 3 wherein the oligomer is a probe.

92. The oligomer of claim 1 wherein the oligomer is a primer.

30 93. The oligomer of claim 3 wherein the oligomer is a primer.

35 94. A pharmaceutical composition, comprising:

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a pharmaceutically acceptable carrier; and  
a therapeutically effective amount of an  
oligomer of claim 1.

5        95. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA duplex or RNA, comprising the steps of:

10        administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 1; and

      allowing the oligomer to have sufficient time  
to bind to the DNA duplex or RNA.

15        96. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA or RNA, the method comprising:

      administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 1; and

20        allowing the oligomer to have sufficient time  
to bind to the DNA or RNA to form a triplex or duplex.

25        97. A method of detecting the presence,  
absence or amount of a particular double stranded or  
single stranded nucleic acid in a biological sample,  
comprising the steps of:

      contacting the sample with an oligomer of claim  
1 under conditions wherein a duplex or a triplex is  
formed between the oligomer and the nucleic acid; and

30        detecting the presence, absence or amount of  
said duplex or triplex.

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98. A method of detecting the presence, absence or amount of a particular single-stranded DNA or RNA in a biological sample, comprising the steps of:

contacting the sample with an oligomer of claim

5 1 under conditions wherein a hybrid duplex is formed  
between the oligomer and the DNA or RNA; and

detecting the presence, absence or amount of said duplex.

10 99. A method of inhibiting expression of at  
least one selected protein in a cell wherein the protein  
is encoded by DNA sequences and the protein is translated  
from RNA sequences, comprising the steps of:

introducing an oligomer of claim 1 into the  
15 cell; and

permitting the oligomer to form a triplex with the DNA or RNA or a duplex with the DNA or RNA whereby expression of the protein is inhibited.

20 100. The method of claim 99 wherein the  
oligomer is introduced into the cell by a method selected  
from the group consisting of calcium phosphate  
transfection, DMSO transfection, dextran transfection,  
electroporation, cationic lipid transfection, anionic  
25 lipid transfection or liposome transfection.

101. A method of introducing an oligomer of claim 1 into cells, comprising:

mixing the oligomer with a permeation enhancing  
30 agent to form a complex; and  
contacting the complex with the cells.

102. A pharmaceutical composition, comprising:

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a pharmaceutically acceptable carrier; and  
a therapeutically effective amount of an  
oligomer of claim 3.

5           103. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA duplex or RNA, comprising the steps of:

10           administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 3; and

              allowing the oligomer to have sufficient time  
to bind to the DNA duplex or RNA.

15           104. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA or RNA, the method comprising:

              administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 3; and

20           allowing the oligomer to have sufficient time  
to bind to the DNA or RNA to form a triplex or duplex.

25           105. A method of detecting the presence,  
absence or amount of a particular double stranded or  
single stranded nucleic acid in a biological sample,  
comprising the steps of:

              contacting the sample with an oligomer of claim  
3 under conditions wherein a duplex or a triplex is  
formed between the oligomer and the nucleic acid; and

30           detecting the presence, absence or amount of  
said duplex or triplex.

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106. A method of detecting the presence, absence or amount of a particular single-stranded DNA or RNA in a biological sample, comprising the steps of:

10 107. A method of inhibiting expression of at  
least one selected protein in a cell wherein the protein  
is encoded by DNA sequences and the protein is translated  
from RNA sequences, comprising the steps of:

introducing an oligomer of claim 3 into the  
15 cell; and

permitting the oligomer to form a triplex with the DNA or RNA or a duplex with the DNA or RNA whereby expression of the protein is inhibited.

20 108. The method of claim 107 wherein the  
oligomer is introduced into the cell by a method selected  
from the group consisting of calcium phosphate  
transfection, DMSO transfection, dextran transfection,  
electroporation, cationic lipid transfection, anionic  
25 lipid transfection or liposome transfection.

109. A method of introducing an oligomer of claim 1 into cells, comprising:

30 mixing the oligomer with a permeation enhancing  
agent to form a complex; and  
contacting the complex with the cells.

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110. A method of introducing an oligomer of  
claim 3 into cells, comprising:

mixing the oligomer with a permeation enhancing  
agent to form a complex; and  
5  
contacting the complex with the cells.

111. A method of synthesizing a desired  
oligomer of claim 1, comprising the steps of:

10  
synthesizing a protected nucleomonomer synthon  
having a protecting group and a base and further having a  
coupling group capable of coupling to a nucleomonomer or  
oligomer;

coupling the nucleomonomer synthon to an  
acceptor nucleomonomer or an acceptor oligomer;

15  
removing the protecting group; and  
repeating the cycle as needed until the desired  
oligomer is synthesized.

112. A method of synthesizing a desired  
20  
oligomer of claim 1, comprising the steps of:

synthesizing a protected oligomer synthon  
having a protecting group and a base and further having a  
coupling phosphite or phosphate group capable of coupling  
to a nucleomonomer or oligomer;

25  
coupling the oligomer synthon to an acceptor  
nucleomonomer or an acceptor oligomer;  
removing the protecting group; and  
repeating the cycle as needed until the desired  
oligomer is synthesized.

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113. The method of claim 111 wherein the  
coupling step is accomplished using hydrogen phosphonate,  
amidite or triester chemistry.

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114. The method of claim 111 wherein the coupling phosphite or phosphate group is selected from the group consisting of hydrogen phosphonate, N,N-diisopropylamino-methylphosphonamidite, N,N-diethylmethylamino-phosphonamidite, N,N-diisopropylamino- $\beta$ -cyanoethoxyphosphine, N,N-diisopropylamino-methoxyphosphine, N,N-diethylamino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino-methoxyphosphine, 2-chlorophenyl phosphate, 4-chlorophenyl phosphate, 2,4-dichlorophenyl phosphate, 2-chlorophenyl thiophosphate, 4-chlorophenyl thiophosphate, 2,4-dichlorophenyl-thiophosphate, and 2,4-dibromophenyl phosphate.

115. A method to synthesize a derivatized oligomer of claim 1 which comprises:

reacting an oligomer containing at least one 5-iodouracil, 5-iodocytosine or N<sup>4</sup>-protected-5-iodocytosine heterocycle with R<sup>2</sup>H in the presence of a Pd catalyst so as to convert said 5-iodouracil, 5-iodocytosine or N<sup>4</sup>-protected-5-iodocytosine to the corresponding 5-R<sup>2</sup> substituted heterocycle.

116. A method of synthesizing a derivatized oligomer of claim 1, comprising the steps of:

synthesizing a protected precursor nucleomonomer synthon having a protecting group and 5-iodouracil or N<sup>4</sup>-protected-5-iodocytosine as a base;

coupling the protected precursor nucleomonomer synthon to an acceptor nucleomonomer or an acceptor oligomer;

removing the protecting group;

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repeating the cycle as needed until the oligomer is synthesized; and

5            derivatizing the precursor nucleomonomer synthon in said oligomer to a derivative having R<sup>2</sup> at the 5-position, where R<sup>2</sup> has the meaning defined in claim 1.

117. A method to evaluate a candidate antisense oligomer for its ability to inhibit gene expression, which method comprises

10            microinjecting said candidate antisense oligomer into a recombinant host cell along with (a) a target vector for the expression of a gene containing a target sequence for said candidate antisense oligomer, and (b) with a control vector for the expression of a 15 control gene encoding a detectable protein, wherein said control gene does not contain said target sequence.

118. The method of claim 117 wherein said target vector is injected at about 2-4 copies per cell 20 and said control vector is injected at about 30-50 copies per cell.

119. The method of claim 117 wherein said detectable protein is chloramphenicol acetyl transferase, 25 luciferase or  $\beta$ -galactosidase.

120. The method of claim 117 wherein said host cell is a mammalian cell.

30            121. A host cell which has been microinjected with (a) a target vector containing an expression system for a gene containing a target sequence for an antisense

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oligomer, (b) a control vector containing an expression system for a detectable protein, and (c) a candidate antisense oligomer.

5 122. A method of amplifying nucleic acid comprising the steps:

mixing the oligomer of claim 1 with a sample containing target nucleic acid;

10 hybridizing the oligomer with the target nucleic acid; and

amplifying the target nucleic acid by PCR or LCR.

123. A method of amplifying nucleic acid comprising the steps:

15 mixing the oligomer of claim 3 with a sample containing target nucleic acid;

hybridizing the oligomer with the target nucleic acid; and

20 amplifying the target nucleic acid by PCR or LCR.

124. The oligomer of claim 1 wherein the oligomer is an antisense oligomer.

25 125. The oligomer of claim 3 wherein the oligomer is an antisense oligomer.

126. The oligomer of claim 1 wherein the oligomer is a triple helix oligomer.

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127. The oligomer of claim 3 wherein the oligomer is a triple helix oligomer.

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